Vincristine (conventional): Drug information

(For additional information see "Vincristine (conventional): Patient drug information" and see "Vincristine (conventional): Pediatric drug information")

For abbreviations and symbols that may be used in Lexicomp (show table)

Special Alerts

Vincristine Sulfate Safety Alert October 2015

Health Canada is notifying health care providers that certain lots of Hospira's vincristine sulfate 1 mg/mL injection (DIN 02183013: 2 mL vial, list #7077A001; 5 mL vial, list #7082A001) have incorrect or outdated safety information on the inner/outer labels and package insert, which may increase the risk to patients and may result in significant patient harm requiring medical intervention. These warnings include:

- Vincristine should only be administered by the intravenous (IV) route. Administration of vincristine by any other route can be fatal.

- Syringes containing this product should be labeled "Warning - for IV use only."

- Extemporaneously prepared syringes containing this product must be packaged in an overwrap which is labeled "Do not remove covering until moment of injection. For IV use only - fatal if given by other routes."

- Contraindication of vincristine in patients with demyelinating Charcot-Marie-Tooth syndrome.

- Potential risk of acute shortness of breath when vincristine is coadministered with mitomycin-C and GI toxicities including necrosis with administration of vincristine.

Health care providers are requested to consult with the approved Canadian product monograph for vincristine sulfate 1 mg/mL for the most updated information. Consumers with questions should contact their health care provider for more information.

ALERT: US Boxed Warning

Experienced physician:

Vincristine should be administered by individuals experienced in the administration of the drug.

Extravasation:

It is extremely important that the intravenous (IV) needle or catheter be properly positioned before any vincristine is injected. Leakage into surrounding tissue during IV administration may cause considerable irritation. If extravasation occurs, discontinue the injection immediately and then introduce any remaining portion of the dose into another vein. Local injection of hyaluronidase and the application of moderate heat to the area of leakage will help disperse the drug and are thought to minimize discomfort and the possibility of cellulitis.

Not for intrathecal use:

For IV use only. Fatal if given by other routes. The intrathecal administration of vincristine usually results in death.

Syringes containing this product should be labeled, using the auxiliary sticker provided, to state, “For intravenous use only. Fatal if given by other routes.” Extemporaneously prepared syringes containing this product must be packaged in an overwrap that is labeled, “Do not remove covering until moment of injection. For intravenous use only. Fatal if given by other routes".

Treatment of patients following intrathecal administration of vincristine has included immediate removal of spinal fluid and flushing with Ringer's lactate solution, as well as other solutions, and has not prevented ascending paralysis and death. In one case, progressive paralysis in an adult was arrested by the following treatment initiated immediately after the intrathecal injection:

As much spinal fluid was removed as could be safely done through lumbar access.

The subarachnoid space was flushed with Ringer's lactate solution infused continuously through a catheter in a cerebral lateral ventricle at the rate of 150 mL/h. The fluid was removed through a lumbar access.

As soon as fresh frozen plasma became available, the fresh frozen plasma, 25 mL, diluted in 1 L of Ringer's lactate solution was infused through the cerebral ventricular catheter at the rate of 75 mL/h with removal through the lumbar access. The rate of infusion was adjusted to maintain a protein level in the spinal fluid of 150 mg/dL.

Glutamic acid 10 g was given IV over 24 hours followed by 500 mg 3 times daily by mouth for 1 month or until neurological dysfunction stabilized. The role of glutamic acid in this treatment is not certain and may not be essential.

Brand Names: US

Vincasar PFS

Brand Names: Canada

Vincristine Sulfate Injection; Vincristine Sulfate Injection USP

Pharmacologic Category

Antineoplastic Agent, Antimicrotubular; Antineoplastic Agent, Vinca Alkaloid

Dosing: Adult

Note: Doses may be capped at a maximum of 2 mg/dose. Dosing and frequency may vary by protocol and/or treatment phase; refer to specific protocol. In order to prevent inadvertent intrathecal administration, the World Health Organization (WHO) and the Institute for Safe Medication Practices (ISMP) strongly recommend dispensing vincristine in a minibag (**NOT** a syringe).

Dosing in the manufacturer’s labeling: IV: 1.4 mg/m^2/dose; frequency may vary based on protocol

Additional dosing in combination therapy; indication-specific and/or off-label dosing:

Acute lymphocytic leukemia (ALL): IV:

Hyper-CVAD regimen: 2 mg/dose days 4 and 11 during odd-numbered cycles (cycles 1, 3, 5, 7) of an 8-cycle phase, followed by maintenance treatment (if needed) of 2 mg monthly for 2 years (Kantarjian, 2004)

CALBG 8811 regimen: Induction phase: 2 mg/dose days 1, 8, 15, and 22 (4-week treatment cycle); Early intensification phase: 2 mg/dose days 15, and 22 (4-week treatment cycle, repeat once); Late intensification phase: 2 mg/dose days 1, 8, 15 (8-week treatment cycle); Maintenance phase: 2 mg/dose day 1 every 4 weeks until 24 months from diagnosis (Larson, 1995)

Central nervous system tumors: IV: PCV regimen: 1.4 mg/m^2/dose (maximum dose: 2 mg) on days 8 and 29 of a 6-week treatment cycle for a total of 6 cycles (van de Bent, 2006) **or** 1.4 mg/m^2/dose (no maximum dose) on days 8 and 29 of a 6-week treatment cycle for up to 4 cycles (Cairncross, 2006)

Hodgkin lymphoma: IV:

BEACOPP regimen: 1.4 mg/m^2/dose (maximum dose: 2 mg) on day 8 of a 21-day treatment cycle (Diehl, 2003)

Stanford-V regimen: 1.4 mg/m^2/dose (maximum dose: 2 mg) in weeks 2, 4, 6, 8, 10, and 12 (Horning, 2000; Horning, 2002)

Non-Hodgkin lymphoma: IV:

Burkitt lymphoma:

CODOX-M/IVAC: Cycles 1 and 3 (CODOX-M): 1.5 mg/m^2 (no maximum dose) days 1 and 8 of cycle 1 and days 1, 8, and 15 of cycle 3 (Magrath, 1996) **or** 1.5 mg/m^2 (maximum dose: 2 mg) days 1 and 8 of cycles 1 and 3 (Mead 2002; Mead 2008); CODOX-M is in combination with cyclophosphamide, doxorubicin, methotrexate, and CNS prophylaxis and alternates with IVAC (etoposide, ifosfamide, mesna, cytarabine, and CNS prophylaxis) for a total of 4 cycles

Hyper-CVAD: 2 mg (flat dose) days 4 and 11 of courses 1, 3, 5, and 7 (in combination with cyclophosphamide, doxorubicin, and dexamethasone) and alternates with even courses 2, 4, 6, and 8 (methotrexate and cytarabine) (Thomas, 2006)

Follicular lymphoma: CVP regimen: 1.4 mg/m^2/dose (maximum dose: 2 mg) on day 1 of a 21-day treatment cycle (in combination with cyclophosphamide and prednisone) for 8 cycles (Marcus, 2005)

Large B-cell lymphoma:

CHOP regimen: 1.4 mg/m^2/dose (maximum dose: 2 mg) on day 1 of a 21-day treatment cycle for 8 cycles (Coiffier, 2002)

EPOCH regimen: 0.4 mg/m^2/day continuous infusion for 4 days (over 96 hours) (total 1.6 mg/m^2/cycle; dose not usually capped) of a 21-day treatment cycle (Wilson, 2002)

Ewing's sarcoma (off-label use): IV: VAC/IE regimen: VAC: 2 mg/m^2 (maximum dose: 2 mg) on day 1 of a 21-day treatment cycle (in combination with doxorubicin and cyclophosphamide), alternates with IE (ifosfamide and etoposide) for a total of 17 cycles (Grier, 2003)

Gestational trophoblastic tumors, high-risk (off-label use): IV: EMA/CO regimen: 1 mg/m^2 on day 8 of 2-week treatment cycle (in combination with etoposide methotrexate, dactinomycin, and cyclophosphamide), continue for at least 2 treatment cycles after a normal hCG level (Escobar 2003; Lurain 2006)

Multiple myeloma (off-label use): IV:

DVD regimen: 1.4 mg/m^2/dose (maximum dose: 2 mg) on day 1 of a 28-day treatment cycle (Rifkin, 2006)

VAD regimen: 0.4 mg/day continuous infusion for 4 days (over 96 hours) (total 1.6 mg/cycle) of a 28-day treatment cycle (Rifkin, 2006)

Ovarian cancer (off-label use): IV: VAC regimen: 1.5 mg/m^2/dose (maximum dose: 2 mg) weekly for 8-12 weeks (Slayton, 1985)

Small cell lung cancer (off-label use): IV: CAV regimen: 1.4 mg/m^2/dose day 1 of a 21-day treatment cycle (Hong, 1989) **or** 2 mg/dose on day 1 of a 21-day treatment cycle (von Pawel, 1999)

Thymoma, advanced (off-label use): IV: ADOC regimen: 0.6 mg/m^2 on day 3 every 3 weeks (in combination with cisplatin, doxorubicin, and cyclophosphamide) (Fornasiero, 1991)

Dosing: Pediatric

(For additional information see "Vincristine (conventional): Pediatric drug information")

Note: Doses may be capped at a maximum of 2 mg/dose. Dosing and frequency may vary by protocol and/or treatment phase; refer to specific protocol. In order to prevent inadvertent intrathecal administration, the World Health Organization (WHO) and the Institute for Safe Medication Practices (ISMP) strongly recommend dispensing vincristine in a minibag (**NOT** in a syringe).

Dosing in the manufacturer's labeling: IV:

Children ≤10 kg: 0.05 mg/kg/dose once weekly

Children >10 kg: 1.5 to 2 mg/m^2/dose; frequency may vary based on protocol

Additional dosing in combination therapy; indication-specific and/or off-label dosing:

Acute lymphocytic lymphoma (ALL): IV: Induction phase: 1.5 mg/m^2/dose days 0, 7, 14, and 21; Consolidation phase: 1.5 mg/m^2/dose days 0, 28, and 56; Delayed intensification phase: 1.5 mg/m^2/dose days 0, 7, and 14; Maintenance phase: 1.5 mg/m^2/dose days 0, 28, and 56 (Bostrom, 2003) **or** Induction phase: 1.5 mg/m^2/dose days 0, 7, 14, and 21; Consolidation phase: 1.5 mg/m^2/dose days 0, 28, and 56; Interim maintenance phases: 1.5 mg/m^2/dose days 0 and 28; Delayed intensification phase: 1.5 mg/m^2/dose days 0, 7, and 14; Maintenance phase: 1.5 mg/m^2/dose every 4 weeks (Avramis, 2002)

Burkitt lymphoma and B-cell ALL: IV: 1.5 mg/m^2 (maximum dose: 2 mg) on days 4 and 11 of initial phase cycle (initial phase is in combination with cyclophosphamide, doxorubicin, and CNS prophylaxis; alternates with secondary phase) for a total of 4 cycles of each phase (Bowman, 1996) **or** 1.5 mg/m^2 (maximum dose: 2 mg) on day 1 of cycle AA (in combination with dexamethasone, ifosfamide, methotrexate, cytarabine, etoposide and CNS prophylaxis) and on day 1 of cycle BB (in

combination with dexamethasone, cyclophosphamide, methotrexate, doxorubicin, and CNS prophylaxis) (Reiter, 1999)

Ewing's sarcoma (off-label use): IV: 2 mg/m^2/dose (maximum dose: 2 mg) on day 1 of a 21-day cycle, administer either every cycle or during odd-numbered cycles (Grier, 2003) **or** 0.67 mg/m^2/day continuous infusion days 1, 2, and 3 (total 2 mg/m^2/cycle; maximum dose/cycle: 2 mg) during cycles 1, 2, 3, and 6 (Kolb, 2003)

Hodgkin lymphoma: IV: BEACOPP regimen: 2 mg/m^2/dose (maximum dose: 2 mg) on day 7 of a 21-day treatment cycle (Kelly, 2002)

Neuroblastoma: IV:

CE-CAdO regimen: 1.5 mg/m^2 (maximum dose: 2 mg) days 1 and 5 every 21 days for 2 cycles (Rubie, 1998) **or** 0.05 mg/kg days 1 and 5 for 2 cycles (Rubie, 2001)

CAV-P/VP regimen (off-label dosing): 0.033 mg/kg/day continuous infusion days 1, 2, and 3, then 1.5 mg/m^2 bolus day 9 of courses 1, 2, 4, and 6 (Kushner, 1994)

Retinoblastoma (off-label use): IV:

Children: 0.05 mg/kg on day 1 every 21 days (in combination with carboplatin) for 8 cycles (Rodriguez-Galindo, 2003)

or

Children ≤36 months: 0.05 mg/kg on day 0 every 28 days (in combination with carboplatin and etoposide) for 6 cycles (Freidman, 2000)

or

Children >36 months: 1.5 mg/m^2 (maximum dose: 2 mg) on day 0 every 28 days (in combination with carboplatin and etoposide) for 6 cycles (Friedman, 2000)

Rhabdomyosarcoma: IV:

VA regimen: 1.5 mg/m^2/dose (maximum dose: 2 mg) weeks 1-8, weeks 13-20, and weeks 25-32 (Crist, 2001)

VAC regimen: 1.5 mg/m^2/dose (maximum dose: 2 mg) weeks 0-12, week 16, weeks 20-25; Continuation therapy: Weeks 29-34, and weeks 38-43 (Crist, 2001)

Wilms' tumor: IV:

Children <1 year: 0.75 mg/m^2/dose weekly for 10-11 weeks, then every 3 weeks for 15 additional weeks (total 25-26 weeks) (Pritchard, 1995)

Children ≥1 year: 1.5 mg/m^2/dose weekly for 10-11 weeks, then every 3 weeks for 15 additional weeks (total 25-26 weeks) (Pritchard, 1995)

or

Children ≤30 kg: 0.05 mg/kg/dose (maximum dose: 2 mg) weeks 1, 2, 4, 5, 6, 7, 8, 10, and 11, followed by 0.067 mg/kg/dose (maximum dose: 2 mg) weeks 12, 13, 18, and 24 (Green, 2007)

Children >30 kg: 1.5 mg/m^2/dose (maximum dose: 2 mg) weeks 1, 2, 4, 5, 6, 7, 8, 10, and 11, followed by 2 mg/m^2/dose (maximum dose: 2 mg) weeks 12, 13, 18, and 24 (Green, 2007)

Dosing: Geriatric Refer to adult dosing.

Dosing: Renal Impairment No dosage adjustment necessary (Kintzel 1995).

Dosing: Hepatic Impairment The manufacturer's labeling recommends the following adjustment: Serum bilirubin >3 mg/dL: Administer 50% of normal dose.

The following adjustments have also been recommended:

Floyd 2006: Serum bilirubin 1.5 to 3 mg/dL or transaminases 2 to 3 times ULN or alkaline phosphatase increased: Administer 50% of dose.

Superfin 2007:

Serum bilirubin 1.5 to 3 mg/dL: Administer 50% of dose.

Serum bilirubin >3 mg/dL: Avoid use.

Dosing: Obesity *ASCO Guidelines for appropriate chemotherapy dosing in obese adults with cancer:* Dose should be capped at a maximum of 2 mg due to neurotoxicity concerns (Griggs 2012)

Dosage Forms Excipient information presented when available (limited, particularly for generics); consult specific product labeling.

Solution, Intravenous, as sulfate:

Vincasar PFS: 1 mg/mL (1 mL, 2 mL)

Solution, Intravenous, as sulfate [preservative free]:

Generic: 1 mg/mL (1 mL, 2 mL)

Generic Equivalent Available (US) Yes

Administration **For IV administration only. FATAL IF GIVEN INTRATHECALLY.**

In order to prevent inadvertent intrathecal administration, the World Health Organization (WHO) and the Institute for Safe Medication Practices (ISMP) strongly recommend dispensing vincristine in a minibag (NOT in a syringe). Vincristine should **NOT** be delivered to the patient at the same time with any medications intended for central nervous system administration.

IV: Preferred administration is as a short 5- to 10-minute infusion in a 25 to 50 mL minibag. If administration via minibag is not possible, may also be administered as a slow (1-minute) push. Some protocols utilize a 24-hour continuous infusion.

Vesicant; ensure proper needle or catheter placement prior to and during infusion. Avoid extravasation.

Extravasation management: If extravasation occurs, stop infusion immediately and disconnect (leave

cannula/needle in place); gently aspirate extravasated solution (do **NOT** flush the line); initiate hyaluronidase antidote; remove needle/cannula; apply dry warm compresses for 20 minutes 4 times a day for 1 to 2 days; elevate (Perez Fidalgo 2012). Remaining portion of the vincristine dose should be infused through a separate vein.

> *Hyaluronidase:* If needle/cannula still in place, administer 1 to 6 mL hyaluronidase (150 units/mL) into the existing IV line; the usual dose is 1 mL hyaluronidase for each 1 mL of extravasated drug (Perez Fidalgo 2012, Schulmeister 2011). If needle/cannula was removed, inject 1 to 6 mL (150 units/mL) subcutaneously in a clockwise manner using 1 mL for each 1 mL of drug extravasated (Schulmeister 2011) **or** administer 1 mL (150 units/mL) as 5 separate 0.2 mL injections (using a 25-gauge needle) subcutaneously into the extravasation site (Polovich 2009).

Hazardous Drugs Handling Considerations

Hazardous agent (NIOSH 2016 [group 1]).

Use appropriate precautions for receiving, handling, administration, and disposal. Gloves (single) should be worn during receiving, unpacking, and placing in storage.

NIOSH recommends double gloving, a protective gown, ventilated engineering controls (a class II biological safety cabinet or a compounding aseptic containment isolator), and closed system transfer devices (CSTDs) for preparation. Double gloving, a gown, and (if dosage form allows) CSTDs are required during administration (NIOSH 2016).

Use Treatment of acute lymphocytic leukemia (ALL), Hodgkin lymphoma, non-Hodgkin lymphomas, Wilms' tumor, neuroblastoma, rhabdomyosarcoma

Use: Off-Label

Ewing’s sarcoma; Gestational trophoblastic tumors (high-risk); Multiple myeloma; Ovarian germ cell tumors; Retinoblastoma (Children); Small cell lung cancer; Thymoma, advanced; Central nervous system tumors; Chronic lymphocytic leukemia (CLL)

Medication Safety Issues

Sound-alike/look-alike issues:

> VinCRIStine may be confused with vinBLAStine, vinorelbine
>
> VinCRIStine conventional may be confused with vinCRIStine liposomal
>
> Oncovin may be confused with Ancobon

High alert medication:

> This medication is in a class the Institute for Safe Medication Practices (ISMP) includes among its list of drug classes which have a heightened risk of causing significant patient harm when used in error.

Geriatric patients: High-risk medication:

Beers Criteria: Vincristine is identified in the Beers Criteria as a potentially inappropriate medication to be used with caution in patients 65 years and older due to its potential to cause or exacerbate syndrome of inappropriate antidiuretic hormone secretion (SIADH) or hyponatremia; monitor sodium concentration closely when initiating or adjusting the dose in older adults (Beers Criteria [AGS 2015]).

Administration issues:

For IV use only. Fatal if administered by other routes. To prevent fatal inadvertent intrathecal injection, it is strongly recommended that vincristine doses be dispensed in a small minibag (25 to 50 mL of a compatible solution), and **NOT** a syringe (ISMP 2014). Vincristine should **NOT** be prepared during the preparation of any intrathecal medications. After preparation, keep vincristine in a location **away** from the separate storage location recommended for intrathecal medications. Vincristine should **NOT** be delivered to the patient at the same time with any medications intended for central nervous system administration.

Adverse Reactions Frequency not defined.

Cardiovascular: Edema, hepatic veno-occlusive disease (SOS; hepatic sinusoidal obstruction syndrome), hypertension, hypotension, ischemic heart disease, myocardial infarction, phlebitis

Central nervous system: Abnormal gait, ataxia, coma, cranial nerve dysfunction (auditory impairment, extraocular muscle impairment, laryngeal muscle impairment, motor dysfunction, paralysis, paresis, vestibular damage, vocal cord paralysis), decreased deep tendon reflex, dizziness, headache, neuralgia (common), neurotoxicity (dose-related), paralysis, paresthesia, parotid pain, peripheral neuropathy (common), seizure, sensorimotor neuropathy, sensory disturbance, vertigo

Dermatologic: Alopecia (common), skin rash

Endocrine & metabolic: Hyperuricemia, uric acid nephropathy (acute), weight loss

Gastrointestinal: Abdominal cramps, abdominal pain, anorexia, constipation (common), diarrhea, intestinal necrosis, intestinal perforation, nausea, oral mucosa ulcer, paralytic ileus, sore throat, vomiting

Genitourinary: Bladder dysfunction (atony), dysuria, urinary retention

Hematologic & oncologic: Anemia (mild), hemolytic uremic syndrome, leukopenia (mild), thrombocytopenia (mild), thrombotic thrombocytopenic purpura

Local: Local irritation (if infiltrated)

Neuromuscular & skeletal: Amyotrophy, back pain, foot-drop, jaw pain, limb pain, myalgia, ostealgia

Ophthalmic: Cortical blindness (transient), nystagmus, optic atrophy with blindness

Otic: Deafness

Renal: Polyuria

Respiratory: Bronchospasm, dyspnea

Miscellaneous: Fever, tissue necrosis (if infiltrated)

<1%, postmarketing, and/or case reports: Anaphylaxis, hypersensitivity reaction, SIADH (syndrome of inappropriate antidiuretic hormone secretion)

Contraindications

Patients with the demyelinating form of Charcot-Marie-Tooth syndrome

Documentation of allergenic cross-reactivity for drugs in this class is limited. However, because of similarities in chemical structure and/or pharmacologic actions, the possibility of cross-sensitivity cannot be ruled out with certainty.

Warnings/Precautions

Concerns related to adverse effects:

• Extravasation: **[US Boxed Warning]: Vincristine is a vesicant; ensure proper needle or catheter placement prior to and during infusion. Avoid extravasation. Individuals administering should be experienced in vincristine administration. Extravasation may cause significant irritation. If extravasation occurs, discontinue immediately and initiate appropriate extravasation management, including local injection of hyaluronidase and moderate heat application to the affected area. Use a separate vein to complete administration.**

• Gastrointestinal effects: Constipation, paralytic ileus, intestinal necrosis and/or perforation may occur; constipation may present as upper colon impaction with an empty rectum (may require flat film of abdomen for diagnosis); generally responds to high enemas and laxatives. All patients should be on a prophylactic bowel management regimen.

• Neurotoxicity: Alterations in mental status such as depression, confusion, or insomnia may occur; neurologic effects are dose-limiting (may require dosage reduction) and may be additive with those of other neurotoxic agents and spinal cord irradiation. Use with caution in patients with pre-existing neuromuscular disease and/or with concomitant neurotoxic agents.

• Respiratory effects: Acute shortness of breath and severe bronchospasm have been reported with vinca alkaloids, usually when used in combination with mitomycin. Onset may be several minutes to hours after vincristine administration and up to 2 weeks after mitomycin. Progressive dyspnea may occur. Permanently discontinue vincristine if pulmonary dysfunction occurs.

• Uric acid nephropathy: Acute uric acid nephropathy has been reported with vincristine.

Disease-related concerns:

• Hepatic impairment: Use with caution in patients with hepatic impairment; dosage modification required. May be associated with hepatic sinusoidal obstruction syndrome (SOS; formerly called veno-occlusive disease [VOD]), increased risk in children <3 years of age; use with caution in hepatobiliary dysfunction. Monitor for signs or symptoms of hepatic SOS, including bilirubin >1.4 mg/dL, unexplained weight gain, ascites, hepatomegaly, or unexplained right upper quadrant pain (Arndt, 2004).

Concurrent drug therapy issues:

• Drug-drug interactions: Potentially significant interactions may exist, requiring dose or frequency adjustment, additional monitoring, and/or selection of alternative therapy. Consult drug interactions database for more detailed information.

Special handling:

• Hazardous agent: Avoid eye contamination.

Other warnings/precautions:

• Not for intrathecal administration: **[US Boxed Warning]: For IV administration only; inadvertent intrathecal administration usually results in death.** To prevent administration errors, the Institute for Safe Medication Practices (ISMP) Targeted Medication Safety Best Practices for Hospitals initiative and the World Health Organization strongly recommend dispensing vincristine diluted in a minibag (ISMP 2014, WHO 2007), **if not dispensed in a minibag, affix an auxiliary label stating "For intravenous use only - fatal if given by other routes" and also place in an overwrap labeled "Do not remove covering until moment of injection."** Vincristine should **NOT** be prepared during the preparation of any intrathecal medications. After preparation, keep vincristine in a location **away** from the separate storage location recommended for intrathecal medications. Vincristine should **NOT** be delivered to the patient at the same time with any medications intended for central nervous system administration.

Metabolism/Transport Effects

Substrate of CYP3A4 (major), P-glycoprotein; **Note:** Assignment of Major/Minor substrate status based on clinically relevant drug interaction potential

Drug Interactions

(For additional information: Launch drug interactions program) Lexicomp®

Aprepitant: May increase the serum concentration of CYP3A4 Substrates. *Risk C: Monitor therapy*

BCG (Intravesical): Immunosuppressants may diminish the therapeutic effect of BCG (Intravesical). *Risk X: Avoid combination*

Bosentan: May decrease the serum concentration of CYP3A4 Substrates. *Risk C: Monitor therapy*

Coccidioides immitis Skin Test: Immunosuppressants may diminish the diagnostic effect of Coccidioides immitis Skin Test. *Risk C: Monitor therapy*

Conivaptan: May increase the serum concentration of CYP3A4 Substrates. *Risk X: Avoid combination*

CYP3A4 Inducers (Moderate): May decrease the serum concentration of CYP3A4 Substrates. *Risk C: Monitor therapy*

CYP3A4 Inducers (Strong): May increase the metabolism of CYP3A4 Substrates. Management: Consider an alternative for one of the interacting drugs. Some combinations may be specifically contraindicated. Consult appropriate manufacturer labeling. *Risk D: Consider therapy modification*

CYP3A4 Inhibitors (Moderate): May decrease the metabolism of CYP3A4 Substrates. *Risk C: Monitor therapy*

CYP3A4 Inhibitors (Strong): May decrease the metabolism of CYP3A4 Substrates. *Risk D: Consider therapy modification*

Dabrafenib: May decrease the serum concentration of CYP3A4 Substrates. Management: Seek alternatives to the CYP3A4 substrate when possible. If concomitant therapy cannot be avoided, monitor clinical effects of the substrate closely (particularly therapeutic effects). *Risk D: Consider therapy modification*

Dasatinib: May increase the serum concentration of CYP3A4 Substrates. *Risk C: Monitor therapy*

Deferasirox: May decrease the serum concentration of CYP3A4 Substrates. *Risk C: Monitor therapy*

Denosumab: May enhance the adverse/toxic effect of Immunosuppressants. Specifically, the risk for serious infections may be increased. *Risk C: Monitor therapy*

Echinacea: May diminish the therapeutic effect of Immunosuppressants. *Risk D: Consider therapy modification*

Enzalutamide: May decrease the serum concentration of CYP3A4 Substrates. Management: Concurrent use of enzalutamide with CYP3A4 substrates that have a narrow therapeutic index should be avoided. Use of enzalutamide and any other CYP3A4 substrate should be performed with caution and close monitoring. *Risk D: Consider therapy modification*

Fingolimod: Immunosuppressants may enhance the immunosuppressive effect of Fingolimod. Management: Avoid the concomitant use of fingolimod and other immunosuppressants when possible. If combined, monitor patients closely for additive immunosuppressant effects (eg, infections). *Risk D: Consider therapy modification*

Fosaprepitant: May increase the serum concentration of CYP3A4 Substrates. *Risk C: Monitor therapy*

Fosphenytoin: May decrease the serum concentration of VinCRIStine. VinCRIStine may decrease the serum concentration of Fosphenytoin. *Risk C: Monitor therapy*

Fusidic Acid (Systemic): May increase the serum concentration of CYP3A4 Substrates. *Risk X: Avoid combination*

Idelalisib: May increase the serum concentration of CYP3A4 Substrates. *Risk X: Avoid combination*

Itraconazole: May enhance the adverse/toxic effect of VinCRIStine. Itraconazole may increase the serum concentration of VinCRIStine. *Risk D: Consider therapy modification*

Leflunomide: Immunosuppressants may enhance the adverse/toxic effect of Leflunomide. Specifically, the risk for hematologic toxicity such as pancytopenia, agranulocytosis, and/or thrombocytopenia may be increased. Management: Consider not using a leflunomide loading dose in patients receiving other immunosuppressants. Patients receiving both leflunomide and another immunosuppressant should be monitored for bone marrow suppression at least monthly. *Risk D: Consider therapy modification*

Lenograstim: Antineoplastic Agents may diminish the therapeutic effect of Lenograstim. *Risk D: Consider therapy modification*

Lopinavir: May increase the serum concentration of VinCRIStine. Management: Monitor closely for signs and symptoms of vincristine toxicity; consider temporary interruption of lopinavir/ritonavir antiviral therapy if patients develop significant toxicity with concurrent use. *Risk D: Consider therapy modification*

Macrolide Antibiotics: May increase the serum concentration of Antineoplastic Agents (Vinca Alkaloids). Macrolides may also increase the distribution of Vinca Alkaloids into certain cells and/or tissues. Management: Consider an alternative to using a macrolide antibiotic when possible in order to avoid the

potential for increased vinca alkaloid toxicity. **Exceptions:** Azithromycin (Systemic); Fidaxomicin; Roxithromycin; Spiramycin. *Risk D: Consider therapy modification*

MiFEPRIStone: May increase the serum concentration of CYP3A4 Substrates. Management: Minimize doses of CYP3A4 substrates, and monitor for increased concentrations/toxicity, during and 2 weeks following treatment with mifepristone. Avoid cyclosporine, dihydroergotamine, ergotamine, fentanyl, pimozide, quinidine, sirolimus, and tacrolimus. *Risk D: Consider therapy modification*

MitoMYcin (Systemic): Antineoplastic Agents (Vinca Alkaloids) may enhance the adverse/toxic effect of MitoMYcin (Systemic). Specifically, the risk of pulmonary toxicity may be increased. *Risk C: Monitor therapy*

Mitotane: May decrease the serum concentration of CYP3A4 Substrates. Management: Doses of CYP3A4 substrates may need to be adjusted substantially when used in patients being treated with mitotane. *Risk D: Consider therapy modification*

Natalizumab: Immunosuppressants may enhance the adverse/toxic effect of Natalizumab. Specifically, the risk of concurrent infection may be increased. *Risk X: Avoid combination*

Netupitant: May increase the serum concentration of CYP3A4 Substrates. *Risk C: Monitor therapy*

NIFEdipine: May increase the serum concentration of VinCRIStine. *Risk C: Monitor therapy*

Nivolumab: Immunosuppressants may diminish the therapeutic effect of Nivolumab. *Risk D: Consider therapy modification*

Ocrelizumab: May enhance the immunosuppressive effect of Immunosuppressants. *Risk C: Monitor therapy*

Palbociclib: May increase the serum concentration of CYP3A4 Substrates. *Risk C: Monitor therapy*

Palifermin: May enhance the adverse/toxic effect of Antineoplastic Agents. Specifically, the duration and severity of oral mucositis may be increased. Management: Do not administer palifermin within 24 hours before, during infusion of, or within 24 hours after administration of myelotoxic chemotherapy. *Risk D: Consider therapy modification*

P-glycoprotein/ABCB1 Inhibitors: May increase the serum concentration of P-glycoprotein/ABCB1 Substrates. P-glycoprotein inhibitors may also enhance the distribution of p-glycoprotein substrates to specific cells/tissues/organs where p-glycoprotein is present in large amounts (e.g., brain, T-lymphocytes, testes, etc.). *Risk C: Monitor therapy*

Phenytoin: May decrease the serum concentration of VinCRIStine. VinCRIStine may decrease the serum concentration of Phenytoin. *Risk C: Monitor therapy*

Pimecrolimus: May enhance the adverse/toxic effect of Immunosuppressants. *Risk X: Avoid combination*

Posaconazole: May enhance the adverse/toxic effect of Antineoplastic Agents (Vinca Alkaloids). Posaconazole may increase the serum concentration of Antineoplastic Agents (Vinca Alkaloids). Management: Avoid the concomitant use of posaconazole and vinca alkaloids when possible. If combined, monitor for increased vinca alkaloid toxicities (eg, neurotoxicity, gastrointestinal toxicity). *Risk D: Consider therapy modification*

Ranolazine: May increase the serum concentration of P-glycoprotein/ABCB1 Substrates. *Risk C: Monitor therapy*

Ritonavir: May increase the serum concentration of VinCRIStine. Management: Monitor closely for signs and symptoms of vincristine toxicity; consider temporary interruption of ritonavir antiviral therapy if patients develop significant toxicity with concurrent use. *Risk D: Consider therapy modification*

Roflumilast: May enhance the immunosuppressive effect of Immunosuppressants. *Risk D: Consider therapy modification*

Sarilumab: May decrease the serum concentration of CYP3A4 Substrates. *Risk C: Monitor therapy*

Siltuximab: May decrease the serum concentration of CYP3A4 Substrates. *Risk C: Monitor therapy*

Simeprevir: May increase the serum concentration of CYP3A4 Substrates. *Risk C: Monitor therapy*

Sipuleucel-T: Immunosuppressants may diminish the therapeutic effect of Sipuleucel-T. *Risk C: Monitor therapy*

St John's Wort: May decrease the serum concentration of CYP3A4 Substrates. Management: Consider an alternative for one of the interacting drugs. Some combinations may be specifically contraindicated. Consult appropriate manufacturer labeling. *Risk D: Consider therapy modification*

Stiripentol: May increase the serum concentration of CYP3A4 Substrates. Management: Use of stiripentol with CYP3A4 substrates that are considered to have a narrow therapeutic index should be avoided due to the increased risk for adverse effects and toxicity. Any CYP3A4 substrate used with stiripentol requires closer monitoring. *Risk D: Consider therapy modification*

Tacrolimus (Topical): May enhance the adverse/toxic effect of Immunosuppressants. *Risk X: Avoid combination*

Teniposide: May enhance the neurotoxic effect of VinCRIStine. *Risk C: Monitor therapy*

Tertomotide: Immunosuppressants may diminish the therapeutic effect of Tertomotide. *Risk C: Monitor therapy*

Tocilizumab: May decrease the serum concentration of CYP3A4 Substrates. *Risk C: Monitor therapy*

Tofacitinib: Immunosuppressants may enhance the immunosuppressive effect of Tofacitinib. Management: Concurrent use with antirheumatic doses of methotrexate or nonbiologic disease modifying antirheumatic drugs (DMARDs) is permitted, and this warning seems particularly focused on more potent immunosuppressants. *Risk X: Avoid combination*

Trastuzumab: May enhance the neutropenic effect of Immunosuppressants. *Risk C: Monitor therapy*

Vaccines (Inactivated): Immunosuppressants may diminish the therapeutic effect of Vaccines (Inactivated). Management: Vaccine efficacy may be reduced. Complete all age-appropriate vaccinations at least 2 weeks prior to starting an immunosuppressant. If vaccinated during immunosuppressant therapy, revaccinate at least 3 months after immunosuppressant discontinuation. *Risk D: Consider therapy modification*

Vaccines (Live): Immunosuppressants may enhance the adverse/toxic effect of Vaccines (Live). Immunosuppressants may diminish the therapeutic effect of Vaccines (Live). Management: Avoid use of live organism vaccines with immunosuppressants; live-attenuated vaccines should not be given for at least 3 months after immunosuppressants. *Risk X: Avoid combination*

Voriconazole: May enhance the adverse/toxic effect of Antineoplastic Agents (Vinca Alkaloids).

Voriconazole may increase the serum concentration of Antineoplastic Agents (Vinca Alkaloids). *Risk D: Consider therapy modification*

Pregnancy Risk Factor

D (show table)

Pregnancy Implications

Animal reproduction studies have demonstrated teratogenicity and fetal loss. May cause fetal harm if administered during pregnancy. Women of childbearing potential should avoid becoming pregnant during treatment.

Breast-Feeding Considerations

It is not known if vincristine is present in breast milk. Due to the potential for serious adverse reactions in the breastfed infant, the decision to discontinue vincristine or to discontinue breastfeeding should take into account the benefits of treatment to the mother.

Monitoring Parameters

Serum electrolytes (sodium), hepatic function tests, CBC with differential, serum uric acid; monitor infusion site; neurologic examination, monitor for constipation/ileus and for signs/symptoms of peripheral neuropathy

Mechanism of Action

Binds to tubulin and inhibits microtubule formation, therefore, arresting the cell at metaphase by disrupting the formation of the mitotic spindle; it is specific for the M and S phases. Vincristine may also interfere with nucleic acid and protein synthesis by blocking glutamic acid utilization.

Pharmacodynamics/Kinetics

Note: In pediatric patients, significant intrapatient and interpatient variability has been reported (Gidding 1999).

Distribution: Rapidly removed from bloodstream and tightly bound to tissues; penetrates blood-brain barrier poorly

Metabolism: Extensively hepatic, via CYP3A4

Half-life elimination: Terminal: 85 hours (range: 19-155 hours)

Excretion: Feces (~80%); urine (10% to 20%; <1% as unchanged drug)

Clearance: In pediatric patients, correlation with diagnosis has been reported; clearance in patients with ALL and non-Hodgkin lymphoma higher than Wilms' tumor (Gidding 1999):

Infants: Vincristine clearance is lower compared to children; more closely related to body weight than to body surface area (Crom1994)

Children and Adolescents 2 to 18 years: Reported means: 357 to 482 mL/minute/m^2; some suggest faster clearance in children <10 years of age than in adolescents (Crom 1994); however, more recent data does not support this finding nor a dosage reduction in adolescent patients (Frost 2003; Gidding 1999)

Pricing: US

Solution (Vincasar PFS Intravenous)

1 mg/mL (1 mL): $18.06

Solution (VinCRIStine Sulfate Intravenous)

1 mg/mL (1 mL): $6.79

Disclaimer: The pricing data provide a representative AWP and/or AAWP price from a single manufacturer of the brand and/or generic product, respectively. The pricing data should be used for benchmarking purposes only, and as such should not be used to set or adjudicate any prices for reimbursement or purchasing functions. Pricing data is updated monthly.

International Brand Names Alcavixin (PH); Biocristin (IN); Cellicristin (LB); Citomid (CR, DO, GT, HN, NI, PA, SV); Citomid RU (MX, TH); Cristol (ET); Criston (BD); Cristovin (IL); Crivosin (CR, DO, GT, HN, NI, PA, SV); Cytocristin (BG, IN, VN, ZW); Farmistin CS (DE); Kyocristine (JP); Oncocristin (CO, PE); Oncovin (AE, AT, AU, BF, BH, BJ, CH, CI, CR, CZ, DE, DK, DO, EE, EG, ET, FI, FR, GB, GH, GM, GN, GR, GT, HN, HR, IE, IT, KE, LR, LU, MA, ML, MR, MT, MU, MW, MX, NE, NG, NI, NL, NO, PA, PK, PL, PT, QA, RU, SA, SC, SD, SE, SK, SL, SN, SV, TN, TR, TZ, UG, ZA, ZM, ZW); Rasteo (ID); Tecnocris (BR); Unicristin (LK); Vinces (AR); Vincran (KR); Vincrina (PY); Vincrisin (BE); Vincristin (HU, PL); Vincristina (IT); Vincristine Delta West (HR); Vincristine Sulfate (PL); Vincristine-David Bull (LU); Vinracine (HK, MY, SG); Vinstin (LK); Vintec (MX)

REFERENCES

1. *American Geriatrics Society 2015 Beers Criteria Update Expert Panel. American Geriatrics Society 2015 updated Beers Criteria for potentially inappropriate medication use in older adults. J Am Geriatr Soc. 2015;63(11):2227-2246. doi: 10.1111/jgs.13702. [PubMed 26446832]*
2. *Arndt C, Hawkins, D, Anderson JR, et al, "Age is a Risk Factor for Chemotherapy-Induced Hepatopathy With Vincristine, Dactinomycin and Cyclophosphamide," J Clin Oncol, 2004, 22(10):1894-901. [PubMed 15143082]*
3. *Aronoff GR, Bennett WM, Berns JS, et al, Drug Prescribing in Renal Failure: Dosing Guidelines for Adults and Children, 5th ed. Philadelphia, PA: American College of Physicians; 2007, p 102, 174.*
4. *Avramis VI, Sencer S, Periclou AP, et al, "A Randomized Comparison of Native Escherichia coli Asparaginase and Polyethylene Glycol Conjugated Asparaginase for Treatment of Children With Newly Diagnosed Standard-Risk Acute Lymphoblastic Leukemia: A Children's Cancer Group Study," Blood, 2002, 99(6):1986-94. [PubMed 11877270]*
5. *Barlogie B, Smith L, and Alexanian R, "Effective Treatment of Advanced Multiple Myeloma Refractory to Alkylating Agents," N Engl J Med, 1984, 310(21):1353-6. [PubMed 6546971]*
6. *Basch E, Prestrud AA, Hesketh PJ, et al; American Society of Clinical Oncology. Antiemetics: American Society of Clinical Oncology clinical practice guideline update. J Clin Oncol. 2011;29(31):4189-4198. [PubMed 21947834]*
7. *Bermudez M, Fuster JL, Llinares E, et al, "Itraconazole-Related Increased Vincristine Neurotoxicity: Case Report and Review of Literature," J Pediatr Hematol Oncol, 2005, 27(7):389-92. [PubMed 16012330]*
8. *Berruti A, Borasio P, Gerbino A, et al, "Primary Chemotherapy With Adriamycin, Cisplatin, Vincristine and Cyclophosphamide in Locally Advanced Thymomas: A Single Institution Experience," Br J Cancer, 1999, 81(5):841-5. [PubMed 10555755]*
9. *Bohme A, Ganser A, and Hoelzer D, "Aggravation of Vincristine-Induced Neurotoxicity by Itraconazole in the Treatment of Adult ALL," Ann Hematol, 1995, 71(6):311-2. [PubMed 8534764]*
10. *Bostrom BC, Sensel MR, Sather HN, et al, "Dexamethasone Versus Prednisone and Daily Oral Versus Weekly Intravenous Mercaptopurine for Patients With Standard-Risk Acute Lymphoblastic Leukemia: A Report from the Children's Cancer Group," Blood, 2003, 101(10):3809-17. [PubMed 12531809]*
11. *Bowman WP, Shuster JJ, Cook B, et al, "Improved Survival for Children With B-Cell Acute Lymphoblastic Leukemia and Stage IV Small Noncleaved-Cell Lymphoma: A Pediatric Oncology Group Study," J Clin Oncol, 1996, 14(4):1252-61. [PubMed 8648381]*
12. *Cairncross G, Berkey B, Shaw E, et al, "Phase III Trial of Chemotherapy Plus Radiotherapy Compared With*

Radiotherapy Alone for Pure and Mixed Anaplastic Oligodendroglioma: Intergroup Radiation Therapy Oncology Group Trial 9402," J Clin Oncol, 2006, 24(18):2707-14. [PubMed 16782910]

13. *Coiffier B, Lepage E, Briere J, et al, "CHOP Chemotherapy Plus Rituximab Compared With CHOP Alone in Elderly Patients With Diffuse Large-B-Cell Lymphoma," N Engl J Med, 2002, 346(4):235-42. [PubMed 11807147]*
14. *Crist WM, Anderson JR, Meza JL, et al, "Intergroup Rhabdomyosarcoma Study-IV: Results for Patients With Nonmetastatic Disease," J Clin Oncol, 2001, 19(12):3091-102. [PubMed 11408506]*
15. *Crom WR, deGraaf SS, Synold T, et al, "Pharmacokinetics of Vincristine in Children and Adolescents With Acute Lymphocytic Leukemia," J Pediatr, 1994, 125(4):642-9. [PubMed 7931891]*
16. *Diehl V, Franklin J, Pfreundschuh M, et al, "Standard and Increased-Dose BEACOPP Chemotherapy Compared With COPP-ABVD for Advanced Hodgkin's Disease," N Engl J Med, 2003, 348(24):2386-95. [PubMed 12802024]*
17. *Donelli MG, Zucchetti M, Munzone E, et al, "Pharmacokinetics of Anticancer Agents in Patients With Impaired Liver Function," Eur J Cancer, 1998, 34(1):33-46. [PubMed 9624235]*
18. *Dupuis LL, Boodhan S, Sung L, et al; Pediatric Oncology Group of Ontario. Guideline for the classification of the acute emetogenic potential of antineoplastic medication in pediatric cancer patients. Pediatr Blood Cancer. 2011;57(2):191-198. [PubMed 21465637]*
19. *Eiden C, Palenzuela G, Hillaire-Buys D, et al, "Posaconazole-Increased Vincristine Neurotoxicity in a Child: A Case Report," J Pediatr Hematol Oncol, 2009, 31(4):292-5. [PubMed 19346885]*
20. *Escobar PF, Lurain JR, Singh DK, et al, "Treatment of High-Risk Gestational Trophoblastic Neoplasia With Etoposide, Methotrexate, Actinomycin D, Cyclophosphamide, and Vincristine Chemotherapy," Gynecol Oncol, 2003, 91(3):552-7. [PubMed 14675675]*
21. *Floyd J, Mirza I, Sachs B, et al, "Hepatotoxicity of Chemotherapy," Semin Oncol, 2006, 33(1):50-67. [PubMed 16473644]*
22. *Floyd JD, Nguyen DT, Lobins RL, et al, "Cardiotoxicity of Cancer Therapy," J Clin Oncol, 2005, 23(30):7685-96. [PubMed 16234530]*
23. *Fornasiero A, Daniele O, Ghiotto C, et al, "Chemotherapy for Invasive thymoma. A 13-year Experience," Cancer, 1991, 68(1):30-3. [PubMed 2049749]*
24. *Friedman DL, Himelstein B, Shields CL, et al, "Chemoreduction and Local Ophthalmic Therapy for Intraocular Retinoblastoma," J Clin Oncol, 2000, 18(1):12-7. [PubMed 10623688]*
25. *Frost BM, Lönnerholm G, Koopmans P, et al, "Vincristine in Childhood Leukaemia: No Pharmacokinetic Rationale for Dose Reduction in Adolescents," Acta Paediatr, 2003, 92(5):551-7. [PubMed 12839283]*
26. *Gidding CE, Meeuwsen-de Boer GJ, Koopmans P, Uges DR, Kamps WA, de Graaf SS. Vincristine pharmacokinetics after repetitive dosing in children. Cancer Chemother Pharmacol. 1999;44(3):203-209. [PubMed 10453721]*
27. *Green DM, Breslow NE, Beckwith JB, et al, "Effect of Duration of Treatment on Treatment Outcome and Cost of Treatment for Wilms' Tumor: A Report From the National Wilms' Tumor Study Group," J Clin Oncol, 1998, 16(12):3744-51. [PubMed 9850017]*
28. *Green DM, Cotton CA, Malogolowkin M, et al, "Treatment of Wilms Tumor Relapsing After Initial Treatment With Vincristine and Actinomycin D: A Report From the National Wilms Tumor Study Group," Pediatr Blood Cancer, 2007, 48(5):493-9. [PubMed 16547940]*
29. *Grier HE, Krailo MD, Tarbell NJ, et al, "Addition of Ifosfamide and Etoposide to Standard Chemotherapy for Ewing's Sarcoma and Primitive Neuroectodermal Tumor of Bone," N Engl J Med, 2003, 348(8):694-701. [PubMed 12594313]*
30. *Griggs JJ, Mangu PB, Anderson H, et al, "Appropriate Chemotherapy Dosing For Obese Adult Patients With Cancer: American Society of Clinical Oncology Clinical Practice Guideline," J Clin Oncol, 2012, 30(13):1553-61. [PubMed 22473167]*
31. *Hong WK, Nicaise C, Larson R, et al, "Etoposide Combined With Cyclophosphamide Plus Vincristine Compared With Doxorubicin Plus Cyclophosphamide Plus Vincristine and With High-Dose Cyclophosphamide Plus Vincristine in the Treatment of Small-Cell Carcinoma of the Lung: A Randomized Trial of the Bristol Lung Cancer Study Group," J Clin Oncol, 1989, 7(4):450-6. [PubMed 2538577]*
32. *Horning SJ, Hoppe RT, Breslin S, et al, "Stanford V and Radiotherapy for Locally Extensive and Advanced Hodgkin's Disease: Mature Results of a Prospective Clinical Trial," J Clin Oncol, 2002, 20(3):630-7. [PubMed 11821442]*
33. *Horning SJ, Williams J, Bartlett NL, et al, "Assessment of the Stanford V Regimen and Consolidative Radiotherapy for*

Bulky and Advanced Hodgkin's Disease: Eastern Cooperative Oncology Group Pilot Study E1492," J Clin Oncol, 2000, 18(5):972-80. [PubMed 10694546]

34. *Institute for Safe Medication Practices. 2014-2015 Targeted Medication Safety Best Practices for Hospitals. Available at http://www.ismp.org/tools/bestpractices/TMSBP-for-Hospitals.pdf. Accessed June 19, 2014.*
35. *Jacobson JO, Polovich M, McNiff KK, et al, "American Society of Clinical Oncology/ Oncology Nursing Society Chemotherapy Administration Safety Standards," J Clin Oncol, 2009, 27(32):5469-75. [PubMed 19786650]*
36. *Kantarjian H, Thomas D, O'Brien S, et al, "Long-Term Follow-Up Results of Hyperfractionated Cyclophosphamide, Vincristine, Doxorubicin, and Dexamethasone (Hyper-CVAD), A Dose-Intensive Regimen, in Adult Acute Lymphocytic Leukemia," Cancer, 2004, 101(12):2788-801. [PubMed 15481055]*
37. *Kelly KM, Hutchinson RJ, Sposto R, et al, "Feasibility of Upfront Dose-Intensive Chemotherapy in Children With Advanced-Stage Hodgkin's Lymphoma: Preliminary Results From the Children's Cancer Group Study CCG-59704," Ann Oncol, 2002, 13(Suppl 1):107-11. [PubMed 12078889]*
38. *Kintzel PE and Dorr RT, "Anticancer Drug Renal Toxicity and Elimination: Dosing Guidelines for Altered Renal Function," Cancer Treat Rev, 1995, 21(1):33-64. [PubMed 7859226]*
39. *Kolb EA, Kushner BH, Gorlick R, et al, "Long-Term Event-Free Survival After Intensive Chemotherapy for Ewing's Family of Tumors in Children and Young Adults," J Clin Oncol, 2003, 21(18):3423-30. [PubMed 12972518]*
40. *Kushner BH, LaQuaglia MP, Bonilla MA, et al, "Highly Effective Induction Therapy for Stage 4 Neuroblastoma in Children Over 1 Year of Age," J Clin Oncol, 1994, 12(12):2607-13. [PubMed 7527454]*
41. *Larson RA, Dodge RK, Burns CP, et al, "A Five-Drug Remission Induction Regimen With Intensive Consolidation for Adults With Acute Lymphoblastic Leukemia: Cancer and Leukemia Group B Study 8811," Blood, 1995, 85(8):2025-37. [PubMed 7718875]*
42. *Legha SS, "Vincristine Neurotoxicity. Pathophysiology and Management," Med Toxicol, 1986, 1(6):421-7. [PubMed 3540519]*
43. *Lurain JR, Singh DK, Schink JC. Primary treatment of metastatic high-risk gestational trophoblastic neoplasia with EMA-CO chemotherapy. J Reprod Med. 2006;51(10):767-772 [PubMed 17086804]*
44. *Magrath I, Adde M, Shad A, et al, "Adults and Children With Small Non-Cleaved-Cell Lymphoma Have a Similar Excellent Outcome When Treated With the Same Chemotherapy Regimen," J Clin Oncol, 1996, 14(3):925-34. [PubMed 8622041]*
45. *Marcus R, Imrie K, Belch A, et al, "CVP Chemotherapy Plus Rituximab Compared With CVP as First-Line Treatment for Advanced Follicular Lymphoma," Blood, 2005, 105(4):1417-23. [PubMed 15494430]*
46. *McCune JS and Lindley C, "Appropriateness of Maximum-Dose Guidelines for Vincristine," Am J Health Syst Pharm, 1997, 54(15):1755-8. [PubMed 9262750]*
47. *Mead GM, Barrans SL, Qian W, et al, "A Prospective Clinicopathologic Study of Dose-Modified CODOX-M/IVAC in Patients With Sporadic Burkitt Lymphoma Defined Using Cytogenetic and Immunophenotypic Criteria (MRC/NCRI LY10 Trial)," Blood, 2008, 112(6):2248-60. [PubMed 18612102]*
48. *Mead GM, Sydes MR, Walewski J, et al, "An International Evaluation of CODOX-M and CODOX-M Alternating With IVAC in Adult Burkitt's Lymphoma: Results of United Kingdom Lymphoma Group LY06 Study," Ann Oncol, 2002, 13(8):1264-74. [PubMed 12181251]*
49. *Morgan C, Tillett T, Braybrooke J, et al, "Management of Uncommon Chemotherapy-Induced Emergencies," Lancet Oncol, 2011, 12(8):806-14. [PubMed 21276754]*
50. *Pérez Fidalgo JA, García Fabregat L, Cervantes A, et al, "Management of Chemotherapy Extravasation: ESMO-EONS Clinical Practice Guidelines," Ann Oncol, 2012, 23(Suppl 7):167-73. [PubMed 22997449]*
51. *Polovich M, Whitford JN and Olsen M, Chemotherapy and Biotherapy Guidelines and Recommendations for Practice, 3rd ed, Pittsburgh, PA: Oncology Nursing Society, 2009.*
52. *Pritchard J, Imeson J, Barnes J, et al, "Results of the United Kingdom Children's Cancer Study Group first Wilms' Tumor Study," J Clin Oncol, 1995, 13(1):124-33. [PubMed 799012]*
53. *Reiter A, Schrappe M, Tiemann M, et al, "Improved Treatment Results in Childhood B-Cell Neoplasms With Tailored Intensification of Therapy: A Report of the Berlin-Frankfurt-Münster Group Trial NHL-BFM 90," Blood, 1999, 94(10):3294-306. [PubMed 10552938]*

54. *Rifkin RM, Gregory SA, Mohrbacher A, et al, “Pegylated Liposomal Doxorubicin, Vincristine, and Dexamethasone Provide Significant Reduction in Toxicity Compared With Doxorubicin, Vincristine, and Dexamethasone in Patients With Newly Diagnosed Multiple Myeloma: A Phase III Multicenter Randomized Trial,” Cancer, 2006, 106(4):848-58. [PubMed 16404741]*

55. *Rodriguez-Galindo C, Wilson MW, Haik BG, et al, "Treatment of Intraocular Retinoblastoma With Vincristine and Carboplatin," J Clin Oncol, 2003, 21(10):2019-25. [PubMed 12743157]*

56. *Roila F, Herrstedt J, Aapro M, et al; ESMO/MASCC Guidelines Working Group. Guideline update for MASCC and ESMO in the prevention of chemotherapy- and radiotherapy-induced nausea and vomiting: results of the Perugia consensus conference. Ann Oncol. 2010;21(suppl 5):v232-v243. [PubMed 20555089]*

57. *Rubie H, Michon J, Plantaz D, et al, “Unresectable Localized Neuroblastoma: Improved Survival After Primary Chemotherapy Including Carboplatin-Etoposide. Neuroblastoma Study Group of the Societe Francaise d'Oncologie Pediatrique (SFOP),” Br J Cancer, 1998, 77(12):2310-7. [PubMed 9649151]*

58. *Rubie H, Plantaz D, Coze C, et al, "Localised and Unresectable Neuroblastoma in Infants: Excellent Outcome With Primary Chemotherapy. Neuroblastoma Study Group, Société Française d'Oncologie Pédiatrique," Med Pediatr Oncol, 2001, 36(1):247-50. [PubMed 11464897]*

59. *Schulmeister L, "Extravasation Management: Clinical Update," Semin Oncol Nurs, 2011, 27(1):82-90. [PubMed 21255716]*

60. *Shields CL, Honavar SG, Meadows AT, et al, "Chemoreduction for Unilateral Retinoblastoma," Arch Ophthalmol, 2002, 120(12):1653-8. [PubMed 12470138]*

61. *Slayton RE, Park RC, Silverberg SG, et al, “Vincristine, Dactinomycin, and Cyclophosphamide in the Treatment of Malignant Germ Cell Tumors of the Ovary. A Gynecologic Oncology Group Study (A Final Report),” Cancer, 1985, 56(2):243-8. [PubMed 2988740]*

62. *Stefanou A and Dooley M, “Simple Method to Eliminate the Risk of Inadvertent Intrathecal Vincristine Administration,” J Clin Oncol, 2006, 21(10):2044. [PubMed 12743160]*

63. *Superfin D, Iannucci AA, and Davies AM, “Commentary: Oncologic Drugs in Patients With Organ Dysfunction: A Summary,” Oncologist, 2007, 12(9):1070-83. [PubMed 17914077]*

64. *Sussman DA, Escalona-Benz E, Benz MS, et al, "Comparison of Retinoblastoma Reduction for Chemotherapy vs External Beam Radiotherapy," Arch Ophthalmol, 2003, 121(7):979-84. [PubMed 12860801]*

65. *Thomas DA, Faderi S, O’Brien S, et al, “Chemoimmunotherapy With Hyper-CVAD Plus Rituximab for the Treatment of Adult Burkitt and Burkitt-Type Lymphoma or Acute Lymphoblastic Leukemia,” Cancer, 2006, 106(7):1569-80. [PubMed 16502413]*

66. *US Department of Health and Human Services; Centers for Disease Control and Prevention; National Institute for Occupational Safety and Health. NIOSH list of antineoplastic and other hazardous drugs in healthcare settings 2016. http://www.cdc.gov/niosh/topics/antineoplastic/pdf/hazardous-drugs-list_2016-161.pdf. Updated September 2016. Accessed October 5, 2016.*

67. *van den Bent MJ, Carpentier AF, Brandes AA, et al, “Adjuvant Procarbazine, Lomustine, and Vincristine Improves Progression-Free Survival But Not Overall Survival in Newly Diagnosed Anaplastic Oligodendrogliomas and Oligoastrocytomas: A Randomized European Organisation for Research and Treatment of Cancer Phase III Trial,” J Clin Oncol, 2006, 24(18):2715-22. [PubMed 16782911]*

68. *Vincasar PFS (vincristine sulfate) [prescribing information]. North Wales, PA: Teva; August 2014.*

69. *Vincristine sulfate [prescribing information]. Lake Forest, IL: Hospira Inc; March 2013.*

70. *von Pawel J, Schiller JH, Shepherd FA, et al. Topotecan versus cyclophosphamide, doxorubicin, and vincristine for the treatment of recurrent small-cell lung cancer. J Clin Oncol. 1999;17(2):658-667. [PubMed 10080612]*

71. *Wilson WH, Grossbard ML, Pittaluga S, et al, “Dose-Adjusted EPOCH Chemotherapy for Untreated Large B-Cell Lymphomas: A Pharmacodynamic Approach With High Efficacy,” Blood, 2002, 99(8):2685-93. [PubMed 11929754]*

72. *World Health Organization, “Vincristine (and Other Vinca Alkaloids) Should Only Be Given Intravenously via a Minibag,” Alert 115, July 2007, World Health Organization, Geneva. Available at http://www.who.int/medicines/publications/drugalerts/Alert_115_vincristine.pdf*

Topic 10045 Version 180.0